REPORT DOCUMENTATION PAGE

AFRL-SR-AR-TR-04-

0160

1. REPORT DATE (DD-MM-YYYY)	2. REPORT TYPE	3. DATES COVERED (From - To)
3/10/04	Final report	12/1/00-11/30/03

4. TITLE AND SUBTITLE
Simulation of Reaction Dynamics for Synthesis of Energetic Materials and Resistant Coatings

5a. CONTRACT NUMBER

5b. GRANT NUMBER
F49620-01-1-0046

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Sharon Hammes-Schiffer

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Pennsylvania State University

Office of Sponsored Programs
110 Technology Center
University Park, PA 16802-1003

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
USAF, AFRL
AFOSR
801 N. Randolph St. Rm 732
Arlington, VA 22203

20040319 115

NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT

Approve for Public Release: Distribution unlimited.

13. SUPPLEMENTARY NOTES

14. ABSTRACT

The objective of this research was the development of theoretical and computational methods to guide the efficient synthesis of HEDM (High Energy Density Matter) for use in advanced propellants and POSS (polyhedral oligomeric silsesquioxanes) for use in coatings resistant to extreme conditions such as heat and abrasion. The research centered on the design of new methodology for the simulation of hydrogen transfer reactions. The projects included the development of the following three types of approaches: grid methods for the calculation of hydrogen vibrational wavefunctions, nonadiabatic molecular dynamics methods for the simulation of proton transfer in liquids, and the nuclear-electronic orbital method for the incorporation of nuclear quantum effects in electronic molecular orbital calculations. The application of these approaches to hydrogen transfer reactions required for the synthesis of HEDM and POSS will provide insight into the detailed mechanisms, as well as the influence of solvent and substituents on the rates and yields. Such mechanistic information will aid in the efficient synthesis of HEDM and POSS and the design of new materials.

15. SUBJECT TERMS
Final Progress

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE		14	19b. TELEPHONE NUMBER (include area code)

Simulation of Reaction Dynamics for Synthesis of Energetic Materials and Resistant Coatings

I. Introduction

The objective of the research supported by this grant was the development of theoretical and computational methods to guide the efficient synthesis of HEDM (High Energy Density Matter) for use in advanced propellants and POSS (polyhedral oligomeric silsesquioxanes) for use in coatings resistant to extreme conditions such as heat and abrasion. The research centered on the design of new methodology for the simulation of hydrogen transfer reactions. The projects included the development of the following three types of approaches: grid methods for the calculation of hydrogen vibrational wavefunctions, nonadiabatic molecular dynamics methods for the simulation of proton transfer in liquids, and the nuclear-electronic orbital (NEO) method for the incorporation of nuclear quantum effects in electronic structure calculations.

II. Methods and Results

A. Grid methods for hydrogen vibrational wavefunctions

The goal of this project was to develop grid-based methodology for the calculation of hydrogen vibrational wavefunctions for systems in which only one or a few specified hydrogen nuclei are treated quantum mechanically.[1,2] We have combined these grid-based methods with electronic structure calculations[3] and with mixed quantum/classical molecular dynamics simulations.[4-7] These approaches are applicable to the hydrogen transfer reactions relevant to the synthesis of HEDM and POSS.

The grid-based methodology we developed to calculate hydrogen vibrational wavefunctions is called the Fourier Grid Hamiltonian Multiconfigurational Self-Consistent-Field (FGH-MCSCF) method.[1] In FGH-MCSCF, the potential energy surface for the transferring hydrogen(s) is calculated on a grid (i.e., all nuclei except the transferring hydrogen(s) are fixed, and the energy is calculated for the hydrogen(s) positioned at each point on the grid). The hydrogen vibrational wavefunctions are calculated by numerically solving the time-independent Schrödinger equation for the hydrogen nucleus (or nuclei) moving on this potential energy surface. We implement an MCSCF approach for the calculation of multidimensional wavefunctions. In this MCSCF approach, the hydrogen vibrational wavefunction is expressed as a linear combination of single configurations that are products of one-dimensional wavefunctions represented directly on the grid. The variational method is utilized to minimize the total energy with respect to both the configuration coefficients and the one-dimensional wavefunctions. Since only a relatively small number of configurations is required for the calculation of accurate hydrogen vibrational wavefunctions, this MCSCF approach avoids the diagonalization of large matrices required for a full configuration interaction approach.

Although the FGH-MCSCF method decreases the computational expense of calculating the vibrational wavefunctions, this grid method requires the calculation of the

potential energy and forces at each grid point. The generation of the grid potential for each molecular dynamics time step is often the bottleneck of mixed quantum-classical molecular dynamics simulations. To decrease the computational expense of this step, we have developed a partial multidimensional grid generation method.[2] This method substantially decreases the number of potential energy calculations (typically by more than an order of magnitude) by avoiding these calculations for grid points with high potential energy. The combination of the FGH-MCSCF and partial multidimensional grid generation methods has been found to accurately describe ground and excited state hydrogen vibrational wavefunctions in a computationally practical manner.

We have used this methodology in two different contexts. First, we have combined electronic structure and hydrogen vibrational wavefunction methods to calculate the hydrogen potential energy surfaces and vibrational wavefunctions for structures along a reaction path obtained from electronic structure methods.[3] These calculations provide useful information about the fundamental nature of the nuclear quantum effects for hydrogen transfer reactions. In addition, we have utilized these grid-based methods for mixed quantum/classical molecular dynamics simulations of hydrogen transfer reactions in condensed phase systems. Specifically, we have studied hydride transfer in liver alcohol dehydrogenase and dihydrofolate reductase enzymes.[4-7]

B. Nonadiabatic molecular dynamics methods for proton transfer in solution

The goal of this project was to develop nonadiabatic mixed quantum/classical molecular dynamics methods for the simulation of proton transfer in solution. The emphasis was on the treatment of both the hydrogen and the donor-acceptor vibrational motion quantum mechanically within the framework of the molecular dynamics with quantum transitions (MDQT) surface hopping approach.[8,9] We applied this method to the model proton transfer reaction $AH-B \rightleftharpoons A^{-}-{}^{+}HB$ in liquid methyl chloride. This project provides the foundation for the simulation of hydrogen transfer reactions required for the synthesis of HEDM and POSS.

In mixed quantum/classical molecular dynamics methods, one or a few nuclei are treated quantum mechanically while the remaining nuclei are treated classically. The MDQT surface hopping method[8,9] incorporates nonadiabatic transitions among the adiabatic vibrational states. The fundamental principle of MDQT is that an ensemble of trajectories is propagated, and each trajectory moves classically on a single adiabatic surface except for instantaneous transitions among the adiabatic states. The adiabatic vibrational states are calculated at each classical molecular dynamics step by solving the time-independent Schrödinger equation for the quantum nuclei. The classical nuclei evolve on the occupied vibrational surface according to Newton's classical equations of motion. Nonadiabatic transitions among these surfaces are incorporated according to a probabilistic algorithm that correctly apportions trajectories among the adiabatic states according to the quantum probabilities (neglecting difficulties with classically forbidden transitions). These quantum probabilities are determined by integration of the time-dependent Schrödinger equation simultaneously with the classical equations of motion. The MDQT method has been applied to proton transfer in solution[9] and in enzymes.[4-6] In these previous applications of MDQT, only the transferring hydrogen motion was treated quantum mechanically.

During the past grant period, we have developed the methodology for treating both the hydrogen motion and the donor-acceptor vibrational motion quantum mechanically within the framework of MDQT.[10] We have applied this methodology to proton transfer in a linear AHB complex. In this case, the treatment of only the hydrogen motion quantum mechanically requires the calculation of one-dimensional wavefunctions, whereas the treatment of both the hydrogen motion and the donor-acceptor vibrational motion quantum mechanically requires the calculation of two-dimensional wavefunctions. We denote the former treatment as a 1D and the latter treatment as a 2D mixed quantum/classical approach.

In the 2D mixed quantum/classical method, the vibrational wavefunctions depend on the proton coordinate r and the AB vibrational coordinate R. For each classical configuration obtained during the molecular dynamics simulation, the two-dimensional time-independent Schrödinger equation is solved numerically on a two-dimensional grid using the grid-based methods described above. The R-grid is generated by moving A and B along the AB axis while maintaining the same orientation and center of mass. The r-grid is generated by moving H along the AB axis. The translational and rotational degrees of freedom of the AHB complex, as well as all solvent degrees of freedom, are treated classically. For 2D MDQT, the nonadiabatic transitions are incorporated among the two-dimensional vibrational states.

We have applied the 2D MDQT approach to the intramolecular reaction $AH-B \rightleftharpoons A^{-}-{}^{+}HB$ in liquid methyl chloride, where AHB represents a phenol-amine complex.[10] This model was initially constructed by Azzouz and Borgis.[11] The aim of our study was to compare the results from 1D and 2D MDQT to elucidate the fundamental issues arising from a quantum mechanical treatment of the donor-acceptor vibrational motion as well as the hydrogen motion. We observed significant differences in the behavior of the systems, particularly in the character of the excited state vibrational wavefunctions. Despite these differences, however, the calculated rates and kinetic isotope effects were qualitatively similar for 1D and 2D MDQT. Thus, these calculations indicate that a classical treatment of the donor-acceptor mode is reasonable for these types of reactions.

C. Nuclear-electronic orbital (NEO) method

The goal of this project was to develop the NEO method for the incorporation of nuclear quantum effects into electronic molecular orbital calculations.[12] In this method, specified nuclei are treated quantum mechanically on the same level as the electrons. Both electronic and nuclear molecular orbitals are expressed as linear combinations of Gaussian basis functions, and the variational method is utilized to minimize the energy with respect to all molecular orbitals, as well as the centers of the nuclear basis functions. Significant correlation effects are included using a multiconfigurational self-consistent-field method. We have applied the NEO approach to the proton transfer reactions required for the synthesis of POSS. This application has illustrated that inclusion of nuclear quantum effects significantly influences the energetics of these hydrogen transfer reactions.

The NEO approach may be used to calculate structures, energies, minimum energy paths, and direct dynamics for chemical reactions. Typically only a subset of the nuclei is treated quantum mechanically. For example, often only the hydrogen nuclei are

chosen for the quantum subsystem, while all other nuclei are included in the classical subsystem. The specified quantum nuclei are treated analogously to the electrons, and properties of the system are averaged over the mixed nuclear-electronic wavefunction. Structures are optimized with respect to only the classical nuclei, and the reaction coordinate along the minimum energy path is comprised of only classical nuclei. Similarly, for dynamical calculations the potential energy surface depends explicitly on only the classical nuclei.

The NEO approach is particularly useful for the description of hydrogen transfer reactions. In this case, the transferring hydrogen nucleus is treated quantum mechanically, and the reaction coordinate of the minimum energy path reflects changes in the environment created by the classical nuclei. This is analogous to the collective solvent coordinate in Marcus theory for electron transfer reactions. The minimum energy path includes nuclear quantum effects such as zero point energy and hydrogen tunneling. This approach maintains the conceptual picture of a reaction path, while eliminating the difficulties associated with large curvature of the reaction path for the transfer of light nuclei.

The NEO approach possesses many advantageous attributes. One important strength of the NEO approach is that the nuclear quantum effects are incorporated during the electronic structure calculation, rather than subsequently calculated as a correction factor. In addition, the NEO approach does not invoke the Born-Oppenheimer separation of the electrons and the quantum nuclei. In the multiconfigurational NEO approach, excited vibrational-electronic states may be calculated, and nonadiabatic effects may be included in dynamical calculations. Finally, the NEO approach is computationally practical for a wide range of chemical reactions, and its accuracy may be improved systematically through increased basis set size and inclusion of additional correlation with larger numbers of configurations and extended methodology.

We are designing the NEO approach to study chemical reactions. As we have shown,[12-14] small basis sets and single configurational wavefunctions are not adequate for describing many chemical reactions, particularly those involving hydrogen transfer, and are limited to the calculation of only ground vibronic states. In the NEO approach, the nuclear basis set is comprised of *s*-type, *p*-type, and *d*-type Gaussian basis functions, and multiple basis function centers for each quantum hydrogen nucleus are allowed. Correlation among electrons and nuclei is included with a procedure analogous to the complete active space self-consistent-field (CASSCF) electronic structure method. The combination of multiple basis function centers and multiconfigurational wavefunctions is required to accurately describe the delocalized, bilobal character of the vibrational wavefunctions involved in hydrogen transfer.[13,14] We have illustrated this requirement through an application of NEO to malonaldehyde.[12,14] We have also benchmarked the NEO method through applications to H_2 and HF and have obtained excellent agreement of the vibrational energy splittings with the experimental values.[12]

In addition, we have developed the methodology to perform a NEO vibrational analysis and have explored the physical implications of such an analysis.[15] This analysis is required for the investigation of chemical reactions on the vibrational-electronic potential energy surface. In the NEO approach, the centers of the nuclear basis functions are optimized variationally on the same level as the coefficients in the molecular orbitals, and the NEO potential energy surface depends explicitly on only the coordinates of the

classical nuclei. The NEO vibrational analysis involves the calculation, projection, and diagonalization of a numerical Hessian to determine the harmonic vibrational frequencies corresponding to the classical nuclei. The analysis of these frequencies allows the characterization of stationary points on the NEO potential energy surface (i.e., distinction among minima, transition states, and higher-order saddle points). This analysis also enables the calculation of zero point energy corrections and thermodynamic quantities such as enthalpy, entropy, and free energy changes for reactions on the NEO potential energy surface. Furthermore, the numerical Hessian may be used in the generation of minimum energy paths, or intrinsic reaction coordinates, on the NEO potential energy surface. We have applied this vibrational analysis to a series of representative molecules, including HCN, the protonated water dimer, and triazene, as well as to the reaction profile for an identity nucleophilic substitution reaction.

The NEO approach has been implemented in the GAMESS electronic structure program.[16] A summary of the current capabilities of our NEO code is as follows:

1. Utilize the DZSPDN nuclear basis set with the option of multiple basis function centers.
2. Calculate expectation values of hydrogen coordinates with respect to molecular orbitals.
3. General options: conventional or direct calculation of integrals, RHF or ROHF treatment of electrons, and the possibility of calculations with symmetry.
4. Treat the quantum nuclei as fermions, bosons, or a mixture of fermions and bosons.
5. Calculate energies and gradients at the NEO-HF level.
6. Calculate, project, and diagonalize the numerical Hessian.
7. Locate and characterize geometry stationary points (i.e., minima and transition states).
8. Calculate zero point energy corrections and thermodynamic properties.
9. Calculate energies at the NEO-CI level.
10. Calculate energies at the NEO-MCSCF level and with state-averaged NEO-MCSCF.
11. Calculate energies at the NEO-MP2 level.

III. Summary

Thus, we have developed three different types of approaches for the simulation of hydrogen transfer reactions. The grid-based methodology enables the efficient calculation of hydrogen vibrational wavefunctions in conjunction with electronic structure calculations and mixed quantum/classical molecular dynamics simulations. The nonadiabatic mixed quantum/classical molecular dynamics method allows the quantum mechanical treatment of both the hydrogen and the donor-acceptor vibrational motion for the simulation of proton transfer in solution. The nuclear-electronic orbital (NEO)

method incorporates nuclear quantum effects in electronic molecular orbital calculations and enables the calculation of structures, energies, minimum energy paths, and direct dynamics for chemical reactions.

The application of these approaches to hydrogen transfer reactions required for the synthesis of POSS and HEDM is providing information that should aid in the efficient synthesis of these materials. These calculations elucidate the role of nuclear quantum effects such as zero point energy and hydrogen tunneling. Moreover, they provide insight into the detailed mechanisms, as well as the influence of solvent and substituents on the rates and yields. Such mechanistic information is critical for the efficient synthesis of POSS and HEDM and the production of new functional species. POSS and HEDM are of interest to the Air Force due to the wide range of technological applications, including advanced propellants and coatings resistant to extreme conditions such as heat and abrasion.

References

[1] S. P. Webb and S. Hammes-Schiffer, Journal of Chemical Physics **113**, 5214 (2000).
[2] T. Iordanov, S. R. Billeter, S. P. Webb, and S. Hammes-Schiffer, Chemical Physics Letters **338**, 389 (2001).
[3] S. P. Webb, P. K. Agarwal, and S. Hammes-Schiffer, Journal of Physical Chemistry B **104**, 8884 (2000).
[4] S. R. Billeter, S. P. Webb, T. Iordanov, P. K. Agarwal, and S. Hammes-Schiffer, Journal of Chemical Physics **114**, 6925 (2001).
[5] S. R. Billeter, S. P. Webb, P. K. Agarwal, T. Iordanov, and S. Hammes-Schiffer, Journal of the American Chemical Society **123**, 11262 (2001).
[6] P. K. Agarwal, S. R. Billeter, and S. Hammes-Schiffer, Journal of Physical Chemistry B **106**, 3283 (2002).
[7] P. K. Agarwal, S. R. Billeter, P. T. R. Rajagopalan, S. J. Benkovic, and S. Hammes-Schiffer, Proc. Natl. Acad. Sci. **99**, 2794 (2002).
[8] J. C. Tully, Journal of Chemical Physics **93**, 1061 (1990).
[9] S. Hammes-Schiffer and J. C. Tully, Journal of Chemical Physics **101** (6), 4657 (1994).
[10] S.-Y. Kim and S. Hammes-Schiffer, Journal of Chemical Physics **119**, 4389 (2003).
[11] H. Azzouz and D. Borgis, Journal of Chemical Physics **98**, 7361 (1993).
[12] S. P. Webb, T. Iordanov, and S. Hammes-Schiffer, Journal of Chemical Physics **117**, 4106 (2002).
[13] M. V. Pak and S. Hammes-Schiffer, Phys. Rev. Lett. (in press).
[14] M. V. Pak, C. Swalina, S. P. Webb, and S. Hammes-Schiffer, Chemical Physics (in press).
[15] T. Iordanov and S. Hammes-Schiffer, Journal of Chemical Physics **118**, 9489 (2003).
[16] M. W. Schmidt, K. K. Baldridge, J. A. Boatz, S. T. Elbert, M. S. Gordon, J. H. Jensen, S. Koseki, N. Matsunaga, K. A. Nguyen, S. Su, T. L. Windus, M. Dupuis, and J. A. Montgomery, Journal of Computational Chemistry **14**, 1347 (1993).

Personnel Supported

Tzvetelin Iordanov (graduate student)
Soo Young Kim (graduate student)
Chet Swalina (graduate student)
Oriol Vendrell (graduate student)
Simon Webb (postdoctoral researcher)
Michael Pak (postdoctoral researcher)
Alexander Soudackov (research associate)
Sharon Hammes-Schiffer (professor)

Publications during funding period (asterisks indicate work supported by AFOSR)

1. P. K. Agarwal, S. P. Webb, and S. Hammes-Schiffer, "Computational studies of the mechanism for proton and hydride transfer in liver alcohol dehydrogenase," *J. Am. Chem. Soc.* **122**, 4803-4812 (2000).
2. * H. Hu, M. N. Kobrak, C. Xu, and S. Hammes-Schiffer, "Reaction path Hamiltonian analysis of dynamical solvent effects for a Claisen rearrangement and a Diels Alder reaction," *J. Phys. Chem. A* **104**, 8058-8066 (2000).
3. A. Soudackov and S. Hammes-Schiffer, "Derivation of rate expressions for nonadiabatic proton-coupled electron transfer reactions in solution," *J. Chem. Phys.* **113**, 2385-2396 (2000).
4. * S. P. Webb, P. K. Agarwal, and S. Hammes-Schiffer, "Combining electronic structure methods with the calculation of hydrogen vibrational wavefunctions: Application to hydride transfer in liver alcohol dehydrogenase," *J. Phys. Chem. B* **104**, 8884-8894 (2000).
5. * S. P. Webb and S. Hammes-Schiffer, "Fourier grid Hamiltonian multiconfigurational self-consistent-field: A method to calculate multidimensional hydrogen vibrational wavefunctions," *J. Chem. Phys.* **113**, 5214-5227 (2000).
6. H. Decornez and S. Hammes-Schiffer, "Model proton-coupled electron transfer reactions in solution: Predictions of rates, mechanisms, and kinetic isotope effects," *J. Phys. Chem. A* **104**, 9370-9384 (2000), featured on the cover.
7. S. Hammes-Schiffer, "Proton-coupled electron transfer," pp. 189-214 in *Electron Transfer in Chemistry Vol. I. Principles, Theories, Methods, and Techniques*, ed. V. Balzani (Wiley-VCH, Weinheim, 2001).
8. S. R. Billeter, S. P. Webb, T. Iordanov, P. K. Agarwal, and S. Hammes-Schiffer, "Hybrid approach for including electronic and nuclear quantum effects in molecular dynamics simulations of hydrogen transfer reactions in enzymes," *J. Chem. Phys.* **114**, 6925-6936 (2001).
9. * T. Iordanov, S. R. Billeter, S. P. Webb, and S. Hammes-Schiffer, "Partial multidimensional grid generation method for efficient calculation of nuclear wavefunctions," *Chem. Phys. Lett.* **338**, 389-397 (2001).
10. S. Hammes-Schiffer, "Theoretical perspectives on proton-coupled electron transfer reactions," *Acc. Chem. Res.* **34**, 273-281 (2001).

11. N. Iordanova, H. Decornez, and S. Hammes-Schiffer, "Theoretical study of electron, proton, and proton-coupled electron transfer reactions in iron bi-imidazoline complexes," *J. Am. Chem. Soc.* **123**, 3723-3733 (2001).
12. Rostov and S. Hammes-Schiffer, "Theoretical formulation for electron transfer coupled to multiple protons: Application to amidinium-carboxylate interfaces," *J. Chem. Phys.* **115**, 285-296 (2001).
13. S. Hammes-Schiffer and S. Billeter, "Hybrid approach for the dynamical simulation of proton and hydride transfer in solution and proteins," *Int. Rev. Phys. Chem.* **20**, 591-616 (2001).
14. M. Kobrak and S. Hammes-Schiffer, "Molecular dynamics simulation of proton-coupled electron transfer in solution," *J. Phys. Chem. B* **105**, 10435-10445 (2001).
15. S. R. Billeter, S. P. Webb, P. K. Agarwal, T. Iordanov, and S. Hammes-Schiffer, "Hydride transfer in liver alcohol dehydrogenase: Quantum dynamics, kinetic isotope effects, and the role of enzyme motion," *J. Am. Chem. Soc.* **123**, 11262-11272 (2001).
16. S. Hammes-Schiffer, "Comparison of hydride, hydrogen atom, and proton-coupled electron transfer reactions," *ChemPhysChem* **3**, 33-42 (2002).
17. P. K. Agarwal, S. R. Billeter, P. T. R. Rajagopalan, S. J. Benkovic, and S. Hammes-Schiffer, "Network of coupled promoting motions in enzyme catalysis," *Proc. Nat. Acad. Sci. USA* **99**, 2794-2799 (2002).
18. P. K. Agarwal, S. R. Billeter, and S. Hammes-Schiffer, "Nuclear quantum effects and enzyme dynamics in dihydrofolate reductase catalysis," *J. Phys. Chem. B* **106**, 3283-3293 (2002).
19. N. Iordanova and S. Hammes-Schiffer, "Theoretical investigation of large kinetic isotope effects for proton-coupled electron transfer in ruthenium polypyridyl complexes," *J. Am. Chem. Soc.* **124**, 4848-4856 (2002).
20. C. Carra, N. Iordanova, and S. Hammes-Schiffer, "Proton-coupled electron transfer in DNA-acrylamide complexes," *J. Phys. Chem. B* **106**, 8415-8421 (2002).
21. * S. Webb, T. Iordanov, and S. Hammes-Schiffer, "Multiconfigurational nuclear-electronic orbital approach: Incorporation of nuclear quantum effects in electronic structure calculations," *J. Chem. Phys.* **117**, 4106-4118 (2002).
22. S. Hammes-Schiffer, "Impact of enzyme motion on activity," *Biochemistry* **41**, 13335-13343 (2002).
23. B. Watney, P. K. Agarwal, and S. Hammes-Schiffer, "Effect of mutation on enzyme motion in dihydrofolate reductase," *J. Am. Chem. Soc.* **125**, 3745-3750 (2003).
24. * T. Iordanov and S. Hammes-Schiffer, "Vibrational analysis for the nuclear-electronic orbital method," *J. Chem. Phys.* **118**, 9489-9496 (2003).
25. S. J. Benkovic and S. Hammes-Schiffer, "A perspective on enzyme catalysis," *Science* **301**, 1196-1202 (2003).
26. * S. Y. Kim and S. Hammes-Schiffer, "Molecular dynamics with quantum transitions for proton transfer: Quantum treatment of hydrogen and donor-acceptor motions," *J. Chem. Phys.* **119**, 4389-4398 (2003).

27. C. Carra, N. Iordanova, and S. Hammes-Schiffer, "Proton-coupled electron transfer in a model for tyrosine oxidation in photosystem II," *J. Am .Chem. Soc.* **125**, 10429-10436 (2003).
28. S. Hammes-Schiffer and N. Iordanova, "Theoretical studies of proton-coupled electron transfer reactions," *Biochim. Biophys. Acta.* (in press).
29. * M. V. Pak and S. Hammes-Schiffer, "Electron-proton correlation for hydrogen tunneling systems," *Phys. Rev. Lett.* (in press).
30. S. Hammes-Schiffer, "Quantum-classical simulation methods for hydrogen transfer in enzymes: Case study of dihydrofolate reductase," *Curr. Opin. Struct. Biol.* (in press).
31. * O. Vendrell, M. Moreno, J. M. Lluch, and S. Hammes-Schiffer, "Molecular dynamics of excited state intramolecular proton transfer: 2-(2′-hydroxyphenyl)-4-methyloxazole in gas phase, solution and protein environments," *J. Phys. Chem. B* (in press).
32. * M. V. Pak, C. Swalina, S. P. Webb, and S. Hammes-Schiffer, "Application of the nuclear-electronic orbital method to hydrogen transfer systems: Multiple centers and multiconfigurational wavefunctions," *Chemical Physics* (in press).
33. S. Hammes-Schiffer, "Kinetic isotope effects for proton-coupled electron transfer reactions" in *Isotope Effects in Chemistry and Biology*, eds. H. Limbach and A. Kohen (Marcel Dekker, Inc., New York, 2004), in press.
34. E. Hatcher, A. V. Soudackov, and S. Hammes-Schiffer, "Proton-coupled electron transfer in soybean lipoxygenase," *J. Am. Chem. Soc.* (in press).

Interactions/Transitions during funding period

a. Presentations during funding period

1. Northwestern University, Evanston, Illinois, December 5, 2000 (physical chemistry seminar): "Proton, Hydride, and Proton-Coupled Electron Transfer Reactions in Solution and Enzymes"
2. University of Wisconsin, Madison, Wisconsin, March 20, 2001 (physical chemistry seminar): "Theoretical Perspectives of Proton-Coupled Electron Transfer"
3. AFOSR Molecular Dynamics and Theoretical Chemistry Contractor's Meeting, Irvine, California, May 21-23, 2001 (invited talk): "Nuclear Quantum Effects in Hydrogen Transfer Reactions for the Synthesis of Polyhedral Oligomeric Silsesquioxanes"
4. CECAM Workshop on New Methods for Combining Born-Oppenheimer Ab Initio Calculations and Empirical Forcefields in Large Scale Simulation Studies, Lyon, France, June 11-13, 2001 (invited talk): "Hybrid Approach for Including Electronic and Nuclear Quantum Effects in the Dynamical Simulation of Hydrogen Transfer in Enzymes"

5. Gordon Research Conference on Enzymes, Coenzymes, and Metabolic Pathways, Meridan, New Hampshire, July 22-26, 2001 (invited talk): "Molecular dynamics studies of the relation between enzyme motion and activity"
6. American Chemical Society National Meeting, Symposium on First Principles Simulation of Chemical Dynamics, Chicago, Illinois, August 26-30, 2001 (talk): "Incorporating Electronic and Nuclear Quantum Effects in the Dynamical Simulation of Proton and Hydride Transfer"
7. American Chemical Society National Meeting, Symposium on Three-Dimensional Silicon-Oxygen Cages: Materials for the 21st Century, Chicago, Illinois, August 26-30, 2001 (invited talk): "Nuclear Quantum Effects in Hydrogen Transfer Reactions for the Synthesis of Polyhedral Oligomeric Silsesquioxanes"
8. American Chemical Society National Meeting, Symposium on Hybrid QM/MM Methods for Large Molecular Systems, Chicago, Illinois, August 26-30, 2001 (invited talk): "Hybrid Approach for Simulating the Dynamics of Proton and Hydride Transfer in Enzymes"
9. Temple University, Philadelphia, Pennsylvania, October 18, 2001 (departmental colloquium): "Molecular Dynamics Studies of the Relation between Enzyme Motion and Activity"
10. Symposium on Structure and Mechanism in Biological Pathways, University Park, Pennsylvania, October 20, 2001 (invited talk): "Molecular Dynamics Studies of the Relation between Enzyme Motion and Activity"
11. Pennsylvania State University, University Park, Pennsylvania, February 15, 2002 (chemical physical seminar): "Molecular Dynamics Studies of the Relation between Enzyme Motion and Activity"
12. Maria Goeppert Mayer Interdisciplinary Symposium, San Diego, California, March 2, 2002 (keynote speaker): "Molecular Dynamics Studies of the Relation between Enzyme Motion and Activity"
13. American Chemical Society National Meeting, Symposium on Structure-Function Correlation in Enzyme Action, Orlando, Florida, April 7-11, 2002 (invited talk): "Molecular Dynamics Studies of the Relation between Enzyme Motion and Activity"
14. American Chemical Society National Meeting, Symposium on Tools for Exploring Potential Energy Surfaces, Orlando, Florida, April 7-11, 2002 (invited talk): "Multiconfigurational Nuclear-Electronic Orbital (NEO) Approach: Including Nuclear Quantum Effects in Electronic Structure Calculations"
15. International Workshop on Quantum Dynamical Concepts: From Diatomics to Biomolecules, Dresden, Germany, April 15-19, 2002 (invited talk): "Hybrid Quantum-Classical Molecular Dynamics of Hydrogen Transfer Reactions"
16. CECAM workshop on Methods for Computer Simulation of Nonadiabatic Charge Transfer Processes in the Condensed Phase, Lyon, France, April 22-24, 2002 (invited talk): "Multiconfigurational Nuclear-Electronic Orbital (NEO) Approach: Including Nuclear Quantum Effects in Electronic Structure Calculations"

17. Great Lakes Regional Meeting of the American Chemical Society, Symposium on Computational Biology, Minneapolis, Minnesota, June 2-4, 2002 (invited talk): "Hybrid Quantum-Classical Molecular Dynamics Studies of the Relation between Enzyme Motion and Activity"
18. Reaction Mechanism Conference, Columbus, Ohio, June 29-July 2, 2002 (invited talk): "Molecular Dynamics Studies of the Relation between Enzyme Motion and Activity"
19. Gordon Research Conference on Computational Chemistry, New London, New Hampshire, June 30-July 5, 2002 (invited talk): "Hybrid Quantum-Classical Molecular Dynamics of Proton and Hydride Transfer Reactions in Enzymes"
20. Workshop on Condensed Phase Dynamics, Telluride, Colorado, July 22-26, 2002 (invited talk): "Multiconfigurational Nuclear-Electronic Orbital (NEO) Approach: Including Nuclear Quantum Effects in Electronic Structure Calculations"
21. Public Lecture, Telluride, Colorado, July 25, 2002 (invited talk): "How Do Biological Enzymes Work?"
22. National American Chemical Society Meeting, Symposium on Classical and Quantum Statistical Mechanics Studies of Solvation, Boston, Massachusetts, August 18-22, 2002 (invited talk): "Theoretical Studies of Proton-Coupled Electron Transfer Reactions in Solution"
23. Rutgers University, Newark, New Jersey, September 13, 2002 (seminar): "Theoretical Perspectives of Proton-Coupled Electron Transfer Reactions"
24. University of California at Berkeley, Berkeley, California, November 12, 2002 (physical chemistry seminar): "Theoretical Perspectives of Proton-Coupled Electron Transfer"
25. Stanford University, Stanford, California, November 13, 2002 (seminar): "Hybrid Quantum-Classical Molecular Dynamics Studies of the Relation between Enzyme Motion and Activity"
26. CIMMS/CALTECH Workshop entitled Molecular Modeling and Computation: Perspectives and Challenges, Caltech, Pasadena, California, November 15-16, 2002 (invited talk): "Hybrid Quantum-Classical Molecular Dynamics of Hydrogen Transfer Reactions in Enzymes"
27. Columbia University, New York, New York, January 31, 2003 (biophysics seminar): "The Impact of Enzyme Motion on Activity"
28. Sanibel Symposium, St. Augustine, Florida, February 22-March 1, 2003 (invited talk): "Hybrid Quantum-Classical Molecular Dynamics of Hydrogen Transfer Reactions in Enzymes"
29. American Chemical Society National Meeting, Symposium on New Electronic Structure Methods: From Molecules to Materials, New Orleans, Louisiana, March 22-26, 2003 (invited talk): "Incorporation of Nuclear Quantum Effects in Electronic Structure Calculations: Multiconfigurational Nuclear-Electronic Orbital Method"
30. American Chemical Society National Meeting, Symposium on Integrating Diverse Computational Approaches to Complex Problem Solving, New Orleans,

Louisiana, March 22-26, 2003 (invited talk): "Hybrid Quantum-Classical Molecular Dynamics of Hydrogen Transfer Reactions in Enzymes"

31. American Chemical Society National Meeting, Symposium on The Cutting Edge: Use of Computers in Teaching and Learning Chemistry, New Orleans, Louisiana, March 22-26, 2003 (invited talk): "Utilization of Computer Movies to Illustrate Quantum Effects and Motion in Enzyme Reactions"
32. American Society of Biochemistry and Molecular Biology National Meeting, Session on Fundamental and Emerging Issues in Enzymatic Catalysis, San Diego, California, April 12-16, 2003 (invited talk): "Impact of Enzyme Motion on Activity"
33. AFOSR Molecular Dynamics Contractor's Meeting, San Diego, California, May 18-20, 2003 (invited talk): "Nuclear Quantum Effects in Hydrogen Transfer Reactions: Polyhedral Oligomeric Silsesquioxanes and Ionic Liquids"
34. Gordon Research Conference on Photosynthesis, New Hampshire, June 22-26, 2003 (invited talk): "Coupling of Electrons and Protons to the Environment"
35. Workshop entitled Radicals in the Rockies, Telluride, Colorado, July 6-12, 2003 (invited talk): "Proton-Coupled Electron Transfer in Solution and Enzymes"
36. International meeting entitled Multidimensional Quantum Reaction Dynamics, Freie Universitat, Berlin, Germany, July 16-18, 2003 (invited talk): "Hybrid Quantum-Classical Calculations of Hydrogen Transfer Reactions"
37. Symposium entitled Computational Modelling of Catalysis, Max Planck Institute, Muelheim, Germany, July 16-18, 2003 (invited talk): "Hybrid Quantum-Classical Molecular Dynamics of Hydrogen Transfer Reactions in Enzymes"
38. Conference entitled Excited State Processes in Electronic and Bio Nanomaterials, Los Alamos, New Mexico, August 11-16, 2003 (invited talk): "Proton-Coupled Electron Transfer Reactions"
39. American Chemical Society National Meeting, Symposium on Making and Breaking Chemical Bonds in Gas and Condensed Phases: Theory and Applications, New York, New York, September 7-11, 2003 (invited talk): "Investigation of Hydrogen Transfer Reactions with the Multiconfigurational Nuclear-Electronic Orbital Method"
40. Central Regional American Chemical Society Meeting, Pittsburgh, Pennsylvania, October 19-23, 2003 (invited talk): "Hybrid Quantum-Classical Molecular Dynamics of Hydrogen Transfer Reactions in Enzymes"
41. University of Iowa, Iowa City, Iowa, November 6, 2003 (colloquium): "Impact of Enzyme Motion on Activity"

b. Consultative and advisory functions

None

c. Transitions

None

New discoveries, inventions, or patent disclosures

None

Honors/Awards

Senior Editor for *The Journal of Physical Chemistry*, January, 2001 - present

Charter Member of the BBCA NIH study section, 2002 - 2006

Vice-Chair/Chair, Theoretical Subdivision of the American Chemical Society, 2002 - 2005

Advisory Board for *Theoretical Chemistry Accounts*, 2002 - present

Alexander M. Cruickshank Lecturer, Gordon Research Conference on Isotopes in Biological & Chemical Sciences, 2004